

Claims

1.A surface glycoprotein comprising the following features:

- (a) it is GPI-anchored on the cell surface;
- (b) it can be removed from the cell membrane by treatment with PI-PLC; and
- (c) its GPI-anchor is characterized by a non-acetylated inositol ring and diacyl glycerol as lipid tail of the anchor.

2.The surface glycoprotein of claim 1 which is the surface glycoprotein ACA characterized by the following additional features:

- (d) it has an isoelectric point of pH 5.5;
- (e) it is present on progenitor cells, granulocytes, monocytes, B-cells (but not T-cells), melanocytes, and other cells; and
- (f) it is preferentially expressed during cell division and in tumor cells;

or a salt, functional derivative or active fraction thereof.

3. The surface glycoprotein ACA of claim 2, obtainable from human blood by

- (a) isolating and lysing cells;
- (b) isolating, disrupting and pelleting the hemoglobin free membrane of said cells;
- (c) repeated salting out of the resuspended membranes with ammonium sulfate (70%; 40% saturation);
- (d) subjecting the proteins precipitated in step (c) to preparative SDS-PAGE under reducing conditions; and
- (e) isolating the gel band of the protein.

4. The surface glycoprotein ACA of claim 2 or 3 having a

molecular weight of about 65 or 68 kD when analyzed by SDS PAGE under reducing conditions.

5. The surface glycoprotein ACA of any one of claims 2 to 4 which contains at least one of the following amino acid sequences:

- (a) D-L-V-P-L-E-D-K-V-T-I-L-G-M-T-A;
- (b) K-L-A-L-S-A-D-D-P-G-F-H-N-F-S-H-Q-R-Q-T;
- (c) D-Q-Q-T-T-S-H-S-S;
- (d) V-L-E-I-M-L-P;
- (e) F-Q-D-E-S-E-A-N-K;
- (f) M-K-Y-V-N-F-K-F-Y-F;
- (g) N-L-D-F-M-T-W-G-V-T-K-V-T-Y-I-G-Q-P-T-G-G;
- (h) L-L-M-D-N-N-E-A-V-H;
- (i) F-D-Q-A-W-A-D-T-A-H-T-W;
- (j) K-L-D-D-I-Q-K-D-M-Y-S-Q-Q-D-T; or
- (k) G-V-W-I-M-K-N-Q-I-T.

6. The surface glycoprotein ACA of any one of claims 2 to 5 which is isolated from blood cells.

7. A process for the isolation of a surface glycoprotein ACA which comprises:

- a) isolating and lysing cells from human blood;
- (b) isolating, disrupting and pelleting the hemoglobin free membrane of said cells;
- (c) repeated salting out of the resuspended membranes with ammonium sulfate (70%; 40% saturation);
- (d) subjecting the proteins precipitated in step (c) to preparative SDS-PAGE under reducing conditions; and
- (e) isolating the gel band of a 65 or 68 kD protein.

8. The surface glycoprotein ACA produced by the process of claim 7.

9. The surface glycoprotein of any one of claims 1 to 6 which is a recombinant protein.

10. The surface glycoprotein of claim 9 which is produced in a mammalian cell.

11. A nucleic acid molecule comprising a nucleotide sequence encoding the surface glycoprotein ACA or a functional derivative or fragment thereof of any one of claims 2 to 7, wherein said surface glycoprotein ACA contains at least one of the following amino acid sequences:

- (a) D-L-V-P-L-E-D-K-V-T-I-L-G-M-T-A;
- (b) K-L-A-L-S-A-D-D-P-G-F-H-N-F-S-H-Q-R-Q-T;
- (c) D-Q-Q-T-T-S-H-S-S;
- (d) V-L-E-I-M-L-P;
- (e) F-Q-D-E-S-E-A-N-K;
- (f) M-K-Y-V-N-F-K-F-Y-F;
- (g) N-L-D-F-M-T-W-G-V-T-K-V-T-Y-I-G-Q-P-T-G-G;
- (h) L-L-M-D-N-N-E-A-V-H;
- (i) F-D-Q-A-W-A-D-T-A-H-T-W;
- (j) K-L-D-D-I-Q-K-D-M-Y-S-Q-Q-D-T; or
- (k) G-V-W-I-M-K-N-Q-I-T.

12. The nucleic acid molecule of claim 11 wherein the nucleotide sequence is a genomic DNA sequence or a cDNA sequence.

13. An expression vector comprising the nucleic acid molecule of claim 11 or 12.

14. A host cell transformed with the expression vector of claim 13.

15. The host cell of claim 14 which is a mammalian host cell.

16. A process for producing a surface glycoprotein ACA comprising the steps of:

- (a) culturing a transformed host cell according to claim 14 or 15 in a suitable culture medium; and
- (b) isolating the protein from the cells or the culture

medium.

17. An antibody to the surface glycoprotein according to any one of claims 1 to 6 or 8 to 10.

18. The antibody of claim 17 which is a monoclonal antibody.

19. A method for the diagnosis of a tumor associated with overexpression of ACA or a predisposition for such a tumor which comprises

(a) contacting a target sample with a compound which is capable of specifically binding (i) to the surface glycoprotein ACA according to any one of claims 2 to 6 or 8 to 10 or (ii) an mRNA transcribed from the nucleic acid molecule of claim 11 or 12 and determining the level of ACA or ACA mRNA; and

(b) comparing the level of ACA protein or ACA-mRNA of the sample determined by use of the compound of step (a) with a control sample obtained from a healthy individual, wherein an elevated level of the surface glycoprotein ACA or the corresponding mRNA is indicative for a tumor or a predisposition for such a tumor.

20. The method of claim 19, wherein the compound is an antibody of claim 17 or 18 or an oligonucleotide which is capable of hybridizing to an mRNA transcribed from the nucleic acid molecule of claim 11 or 12.

21. A pharmaceutical composition containing a compound capable of reducing or eliminating (a) the expression of the nucleic acid sequence encoding the surface glycoprotein ACA and/or (b) the biological activity of ACA.

22. Use of a compound capable of reducing or eliminating (a) the expression of the nucleic acid sequence encoding the surface glycoprotein ACA and/or (b) the biological activity of ACA for the preparation of a pharmaceutical for

the treatment of cancer or prophylaxis.

23. The method of claim 19 or 20 or the use according to claim 22, wherein the cancer is a melanoma, leukemia, renal cancer, lung cancer, breast cancer, colon cancer, gastric cancer, or any other form of cancer.

24. A kit containing the antibody of claim 17 or 18 or an oligonucleotide which is capable of hybridizing to an mRNA transcribed from the nucleic acid molecule of claim 11 or 12.